## DETAILED ACTION

Responsive to communications entered 6/19/2007 Claims 1-20 are pending. Claims 6,7,12-15,20 stand withdrawn. Claims 1-5,8-11,16-19 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Priority*

This application is a DIV of 09/843,949 filed 04/30/2001 (now PAT 6,642,052) which is a CIP of 09/258,209 filed 02/25/1999 (now PAT 6,291,226).

### *Withdrawn Objection(s) and/or Rejection(s)*

The objection to claims 2-20 for being dependent on a non-existent claims is hereby withdrawn in view of applicant's amendments to the claims.

The rejection of claim 1 under 35 U.S.C. 102(e) as being anticipated by Massie et al (US Patent 6,291,226) is hereby withdrawn in view of applicants successful petition to accept an unintentionally delayed claim under 35 U.S.C. § 120 for the benefit of priority to prior-filed nonprovisional application 09/258,209 filed 02/25/1999.

### *Election/Restrictions*

Claims 2-5,8-11,16-19 are hereby rejoined in view of the claims no longer being dependent on non-existent claims.

Applicant's election without traverse of E1 for the species of transcriptional region in the reply filed on 6/19/2007 is acknowledged.

Applicant's election without traverse of dicistronic for the species of expressible DNA cassette in the reply filed on 6/19/2007 is acknowledged.

Applicant's election without traverse of antisense RNA for the species of expressible exogenous DNA in the reply filed on 6/19/2007 is acknowledged.

Applicant's election without traverse of $10^3$ for the species of number of clones in the reply filed on 6/19/2007 is acknowledged.

Claims 6-7,12-15,20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/19/2007.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Armentano et al** (US Patent 5,707,618) in view of **Vogels et al** (US Patent 6,340,595).

The claimed subject matter is drawn to an adenoviral expression library comprising:

a plurality of recombinant adenoviruses, each recombinant adenovirus being deleted for an essential gene of a late transcriptional region of adenoviral genome and having the essential gene expressibly cloned in a second transcriptional region of adenoviral genome, each recombinant adenovirus further comprising an expressible piece of exogenous DNA.

**Armentano et al** teach, throughout the document and especially claim 1 and the example, preparation of a plurality of recombinant adenovirus vectors comprising a deleted E1 transcription region and in which the protein IX gene has been relocated to transcription region E4.

Figure 1 of Armentano et al indicates protein IX is transcribed late, thus said "relocation" of the protein IX gene reads on "adenoviruses being deleted for an essential gene of a **late** transcriptional region of adenoviral genome and having the essential gene expressibly cloned in a second transcriptional region of adenoviral genome." Emphasis Added. Armentano et al teach in column 3, lines 33-35, an embodiment comprising a heterologous gene of mammalian origin under control of a eukaryotic transcription promoter, which is taken as "each recombinant adenovirus further comprising an expressible piece of exogenous DNA."

Armentano et al do not teach a library of adenoviruses, such as set forth in the preamble of claim 1.

**Vogels et al** teach, throughout the document and especially the title and abstract, adenoviral libraries directed toward determining the function of various gene products such as polypeptides, antisense nucleic acids and genetic suppressor elements (GSEs).

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use the adenoviruses bearing relocated genes per Armentano et al as the vector for the library of Vogels et al.

One of ordinary skill in the art would have been motivated to use the adenoviruses bearing relocated genes per Armentano et al as the vector for the library of Vogels et al because adenoviruses with relocated genes represent safer vectors, being unable to generate replication-competent adenoviruses (RCAs), as noted by Armentano et al in the abstract. In fact, Vogels et al state in column 3, line 56 the libraries are preferably RCA free.

One of ordinary skill in the art would have had a reasonable expectation of success in employing the adenoviruses bearing relocated genes per Armentano et al as the vector for the library of Vogels et al because both references concern manipulation of the adenovirus genome, thus the adenovirus vectors of Armentano et al lies well within the scope of Vogels et al.

Claims 2-5,16,17,19 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Armentano et al** (US Patent 5,707,618) in view of **Vogels et al** (US Patent

6,340,595) as applied to claim 1 above, and further in view of **Webster et al** (1994 J. Virology 68:7292-7300).

**Armentano et al in view of Vogels et al** is relied on as above.

Said relocation of the protein IX gene to E4, as set forth in Armentano et al (mentioned above) is taken as meeting the limitation of the early transcription region of claim 3.

In addition, Armentano et al teach an alternative embodiment in column 6, lines 4-5 wherein the ORF6 gene from E4 is relocated to E1 (elected species), as set forth in claims 4 and 5.

Vogels et al teach in claim 27, DNA libraries, as set forth in claim 16.

Vogels et al teach in example 16, vectors for expressing antisense RNA (elected species), as set forth in claim 17.

Vogels et al teach in column 50, line 20 0.7-0.8 x $10^9$ plaque forming units (pfu), which is taken as representing at least 1000 clones, as set forth in claim 19.

Armentano et al in view of Vogels et al do not teach relocation of the essential gene encoding adenovirus protease (claim 2).

**Webster et al** teach, throughout the document and especially the first sentence of the abstract that adenovirus protease is essential.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to relocate the essential adenovirus protease gene per Webster et al to form RCA free adenovirus vectors per Armentano et al in view of Vogels et al.

One of ordinary skill in the art would have been motivated to relocate the essential adenovirus protease gene per Webster et al to form RCA free adenovirus vectors per Armentano et al in view of Vogels et al because Armentano mention in column 6, lines 55-60 that the gene relocation strategy is compatible with any essential adenovirus gene.

One of ordinary skill in the art would have had a reasonable expectation of success in moving the adenovirus protease of Webster et al to form RCA free adenovirus vectors per Armentano et al in view of Vogels et al because all three references concern various genes of the adenovirus genome, thus the adenovirus protease gene of Webster et al lies well within the scope of RCA free adenovirus vectors according Armentano et al in view of Vogels et al.

Claims 8-11,18 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Armentano et al** (US Patent 5,707,618) **in view of Vogels et al** (US Patent 6,340,595) **further in view of Webster et al** (1994 J. Virology 68:7292-7300), as applied to claims 2-5,16,17,19 above and further in view of **Bailey et al** (US Patent 6,274,341).

**Armentano et al in view of Vogels et al further in view of Webster et al** is relied on as above.

**Armentano et al in view of Vogels et al further in view of Webster et al** do not teach: dicistronic cassettes (claim 8, elected species); an Internal Ribosome Entry Site (IRES) (claim 18; elected species) and a regulatable promoter such as a tetracycline-inducible promoter (claims 9-11).

**Bailey et al** teach, throughout the document and especially figure 1a tetracycline inducible promoter governing a dicistronic transcription cassette including a cytostatic gene and an IRES.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to add the tetracycline inducible promoter governing a dicistronic transcription cassette including a cytostatic gene with an IRES of Bailey et al to the adenovirus vector library bearing a relocated protease gene per Armentano et al in view of Vogels et al further in view of Webster et al.

One of ordinary skill in the art would have been motivated to add the tetracycline inducible promoter governing a dicistronic transcription cassette including a cytostatic gene with an IRES of Bailey et al to the adenovirus vectors bearing a relocated protease gene per Armentano et al in view of Vogels et al further in view of Webster et al because the cytostatic gene provides for increased production of gene products by inducibly arresting cell proliferation, which is useful for recombinant gene expression according to Bailey in the abstract.

One of ordinary skill in the art would have had a reasonable expectation of success in adding the tetracycline inducible promoter governing a dicistronic transcription cassette including a cytostatic gene of Bailey et al to the adenovirus vectors bearing a relocated protease gene per Armentano et al in view of Vogels et al further in view of Webster et al because Bailey et al mention in column 12 lines 37-41 that a preferred viral gene delivery system includes adenoviruses that have been manipulated in such that they encode a gene product of interest but is inactivated in

terms of their ability to replicate in a normal lytic viral life cycle, which falls squarely in the scope of technology according to Armentano et al in view of Vogels et al further in view of Webster et al.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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